

Oral metastatic clear-cell tumours: To and fro: Unusual case reports

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Abstract

We report two extremely rare cases of metastatic clear-cell carcinomas, which metastasized from and to the oral cavity and both presented clinically in the oral cavity. First case was a primary lesion in the oral cavity, which showed distant metastatic deposits in liver, kidney, bone and brain. Histopathologically, lobules of pleomorphic clear cells were evident descending from the overlying mucosa, raising the suspicion of renal cell carcinoma. Immunohistochemical staining for CD10 was negative and the case was diagnosed as clear-cell type of oral squamous cell carcinoma which had disseminated to distant organs. In the second case, dysplastic clear granular cells were seen invading the bone. Immunohistochemical staining for CD10 showed focal mild positivity, confirming the diagnosis as clear-cell renal carcinoma which had metastasized to the oral cavity. Metastatic tumours must be considered in the differential diagnosis of rapidly growing ulcero proliferative lesions in the oral cavity.

Keywords: Clear cells, metastatic tumours, oral squamous cell carcinoma

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INTRODUCTION

In histological section, a clear cell is a cell that shows clear cytoplasm when stained with hematoxylin and eosin (H&E). There are diverse group of clear-cell tumours of the oral mucosa, salivary glands and jaws behaving according to their origin, for example, odontogenic, salivary gland and metastatic. The cytoplasm of cells in these tumours appear clear because of aggregation of water, glycogen, intermediate filaments or immature zymogen granules, or a deficiency of cellular organelles.^[1,2] The World Health Organization acknowledges clear-cell squamous cell carcinoma as a distinct entity at sites such as penis and skin but not in the head and neck area. Noteworthy, they are notorious to be more destructive if found in other locations,

including oral cavity.^[3] Kuo in 1980^[4] first described clear-cell squamous cell carcinoma (CCSCC) which is still very scarcely reported in literature. The clear-cell appearance is attributable to hydropic degeneration of neoplastic cells and the accumulation of intracellular fluid, not the accumulation of glycogen, lipid or mucin. All cases of CCSCC cases which were located in head and neck region, were usually found in the mandible with very few cases present in maxilla.^[5] However, in our patient, the site was maxilla showing nodulo-ulcerative growth.

Metastatic neoplasms to the oral cavity are exceedingly rare and constitute nearly 1% of all oral malignancies. In these cases, metastatic deposits may be located in bone

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or the oral soft tissues.^[6] Renal cell carcinoma (RCC) has high metastatic probability, with a very poor prognosis. Early diagnosis of these lesions is a prerequisite for an optimum and a favourable cure. It is very uncommon to find metastasis of RCC to the oral cavity and it is even more infrequent to be located on buccal mucosa. Quite significantly, in 23% of the cases, the distant organ progression of the disease is the first manifestation of an unknown primary lesion. Metastatic breast carcinomas have been documented to be the most often occurring metastasis to the oral cavity, followed by lung and renal malignancies. The feasible course of metastasis to the oral cavity includes arterial, venous and lymphatic circulations. Various hypotheses have been proposed to account for head and neck metastasis without lung association and pulmonary vascular filtration. Such exceptional cases usually manifest disseminated metastasis to liver, lungs, bone and brain. RCCs are typically characterized by rich vascular network thus accelerating hematogenous extension and the occurrence of remote metastasis. The most important hematogenous extension route in RCC is the vena cava system, which leads to the lung. The most plausible explanation is that tumour cells bypass the filtration of the lungs, probably through the valveless vertebral venous plexus.

These comprise spread via Batson's venous plexus or through the thoracic lymphatic duct.^[6-8] The following case presentations are the intriguing case studies of two patients, first case with distant metastasis from the oral cavity and the second case of distant metastasis of clear-cell renal adenocarcinoma to the oral cavity.

CASE PRESENTATION

Case report 1

A 55-year-old male patient reported to Dental OPD with a complaint of a large swelling of one month duration in left gingival region extending to the right posterior tooth region obliterating the buccal vestibule. The lesion was painful and patient had difficulty in mastication and opening the mouth. As per the patient's statement, he got his left side maxillary molar extracted one month back by a local dentist in his hometown. Within a few days after extraction, he noticed a persistently growing swelling in the left vestibular area extending anteriorly till distal to lateral incisor and posterior till tuberosity which attained a large size (Approximately 4 cm × 4 cm) within a span of one month. On clinical examination, the swelling was noduloulcerative and firm, however, tender on palpation, bled on touch and non-pulsatile with colour similar to adjacent gingiva [Figure 1]. On extraoral



Figure 1: Nodule like ulcero-proliferative growth seen in maxillary posterior region bilaterally [Case1].

examination, no gross facial asymmetry was observed. Quite incomprehensibly, similar ulcero proliferative growth of size 2 × 2 cm, not associated with bleeding on touch, was present in the right side in relation to maxillary canine till first premolar region. There was bilateral obliteration of buccal vestibule in maxillary arch [Figure 1].

On right side, submandibular lymph node was palpable of size 2 cm, tender, but not fixed to underlying structures. While on the left side also, submandibular lymph node was fixed and tender. Considering the clinical features of the lesion, provisional clinical diagnosis was gingival hyperplasia, squamous cell carcinoma and metastatic disease.

Investigations like complete blood picture, differential leukocyte count, peripheral blood smear and coagulation profile were done. Subsequently, the incisional biopsy was done and submitted to the Department of Oral and Maxillofacial Pathology. Meanwhile, it came to our knowledge that within few days of reporting to the Dental OPD, the patient had to be admitted in Intensive care unit of our Institute because of seizures. As per the patient's family recorded statement, this was the first incidence when the patient had convulsions. Magnetic Resonance Imaging MRI of brain was done and metastatic deposits were observed. Further, cone beam computed tomography revealed possibility of hepatic, renal, brain and bony metastasis, implying the patient already had disseminated disease. [Figure 2a and b]. Multiple lytic lesions with soft tissue component were noted in visualized vertebrae, sacrum, ileum, left femur, right 7th, 10th and 11th ribs [Figure 2c]. Further, pathological fracture of 11th rib was noted along with bilateral pleural effusion with passive atelectasis of basal lung. MRI study of brain exhibited multiple

rounds to oval altered signal intensity areas, suggestive of metastatic areas. Cone-beam Computed Tomography CBCT investigation showed moth eaten appearance of bony destruction in the maxilla [Figure 3]. Histopathologic findings revealed clear-cell degenerative changes in the overlying oral mucosa. Large clusters and sheets of clear cells showing abundant clear cytoplasm, and dysplastic features like pleomorphism and hyperchromatism of cells were prominently observed in the connective tissue stroma [Figures 4 and 5]. Clinical observations and results of the investigations strongly pointed towards metastatic renal cell carcinoma. However, microscopically, the sheets of dysplastic clear cells were connected to overlying mucosa raising the suspicion of disseminated oral squamous cell carcinoma. Therefore, immunohistochemical staining by renal cell tumour marker CD10 was carried out which came out to be negative. Periodic acid Schiff and mucicarmine staining was also done and was found to be negative ruling out the neoplasm of salivary gland or odontogenic origin. After careful evaluation of clinical, histopathological and immunohistochemical findings, we diagnosed the lesion as squamous cell carcinoma (Clear-cell type). The patient succumbed to disease within a span of one month in the hospital during treatment.

Case 2

A 26-year-old male presented with a profusely bleeding periapical cystic lesion in upper maxillary central incisor region. Patient did not give history of tobacco smoking, chewing and alcohol consumption. On eliciting the detailed history, it was revealed that patient was undergoing chemotherapy for suspected carcinoma of

the abdomen. There was no cervical lymphadenopathy. Biopsy of the lesion revealed organoid arrangement of clear cells resembling vegetable-like configuration, and showing well-defined cytoplasmic membrane, indicative of renal cells [Figure 6a]. In some areas, pleomorphic and hyperchromatic clear cells were also evident surrounded by rich vascular network. Other very significant finding was that the tumour cells were invading bone and osteoclasts were also seen, suggesting it to be an osteolytic lesion [Figure 6(b)]. Histopathologic findings along with clinical observations made us suspect it as a metastatic case of renal cell carcinoma. Immunohistochemistry was done using renal tumour marker CD10, which exhibited focal and mild positivity, favouring the diagnosis of metastatic renal cell carcinoma [Figure 7a and b]. Unfortunately, the patient did not come again to collect his report and probably shifted to some other hospital for further treatment.

DISCUSSION

We report two cases of metastatic clear-cell carcinomas, similar microscopically and clinically yet showing different location of the primary lesion, first case being disseminated clear-cell oral squamous cell carcinoma, (T4 N2 M1, Stage 1V) and the other case of clear-cell renal carcinoma showing distant metastases to the oral cavity.

Microscopically, differential diagnosis of clear-cell neoplasms in oral cavity region comprise salivary gland origin (mucoepidermid carcinoma, acinic cell carcinoma, epithelial-myoepithelial carcinoma, clear-cell myoepithelial carcinoma, and hyalinizing clear-cell carcinoma), odontogenic source (clear-cell odontogenic

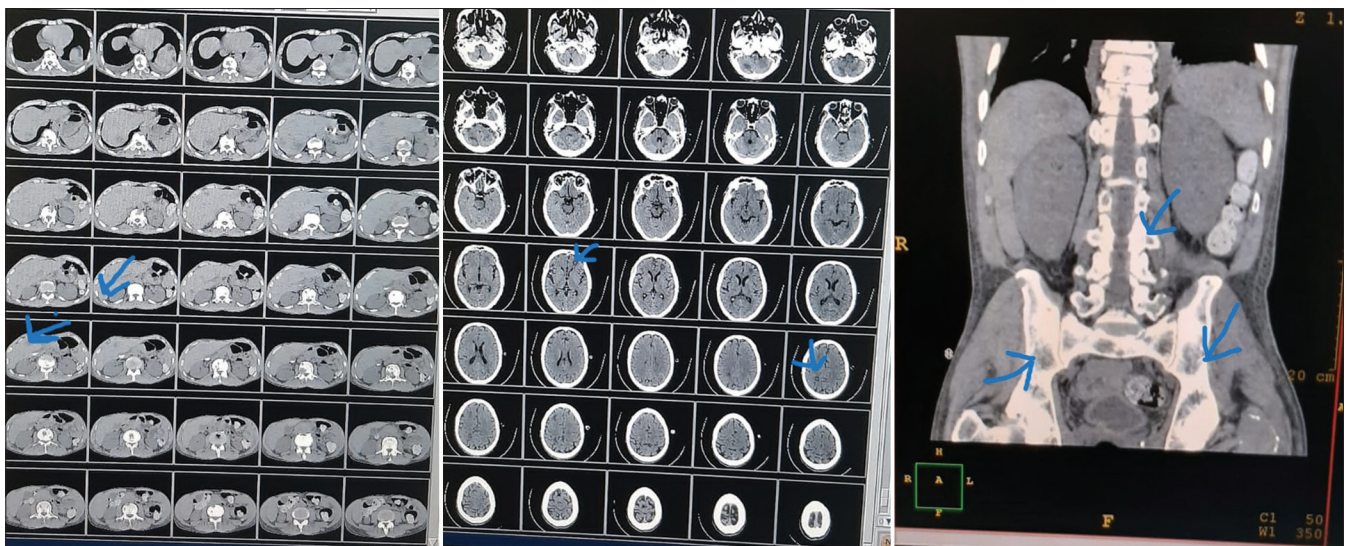


Figure 2: (a) Non-contrast CT abdomen: multiple hypodense lesions can be appreciated in the liver. (b) Non-contrast CT Head-two hyperdense lesions surrounded by edema seen in the cerebral cortex (c) Non-contrast CT abdomen sagittal plane shows moth-eaten appearance in the pelvic bones is visualised



Figure 3: CBCT image shows moth-eaten bony destruction of maxilla [Case 1]

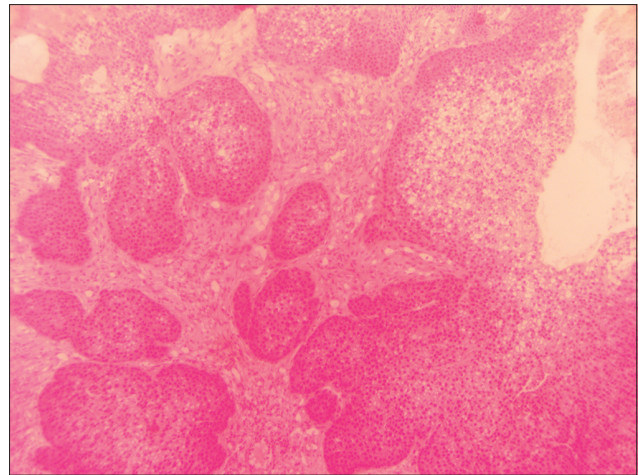


Figure 4: Hematoxylin and eosin staining shows dysplastic overlying mucosa and invading islands of pleomorphic clear cells in the connective tissue stroma (x100) [Case 1]

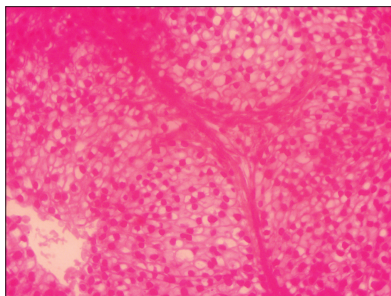


Figure 5: Hematoxylin and eosin staining shows clusters of clear cells (X400) [Case 1]

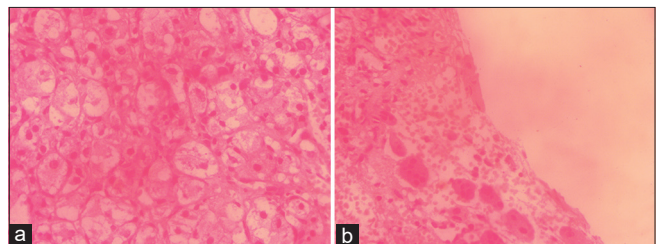


Figure 6: (a) Hematoxylin and eosin staining shows pleomorphic polygonal clear and granular cells arranged in lobules (X400) [Case 2] (b) Hematoxylin and eosin staining shows osteoclasts (X400) [Case 2]

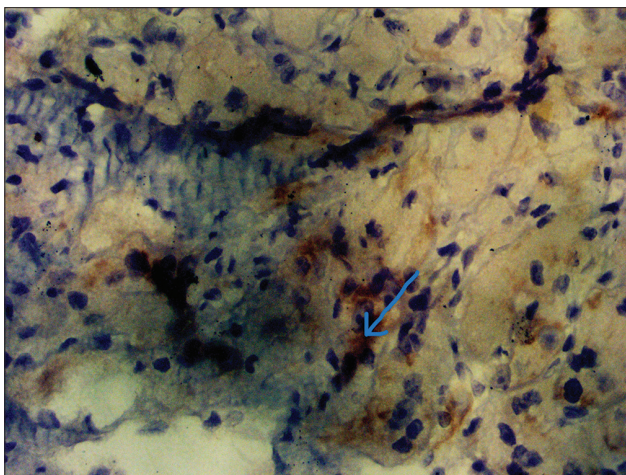


Figure 7: (a) Immunohistochemical staining with CD10 exhibited focal positivity (X400) [Case 2] (b) Immunohistochemical staining with CD10 exhibited focal positivity (X400) [Case 2]

carcinoma and clear odontogenic ghost-cell tumour) and metastatic renal clear-cell carcinoma.^[9,10]

The distinction of a metastatic tumour from a primary malignancy is arduous for even an experienced pathologist and commands special staining, immunohistochemical markers and electron microscopy to identify the primary tumour.^[11]

PAS and mucicarmine staining was negative in first case ruling it out as salivary gland malignancy. Possibility of renal cell carcinoma was negated as immunohistochemical staining for CD10 was found to be negative. The present case did not show typical histopathological features of clear-cell odontogenic carcinoma like biphasic population of cells characterized by polygonal, clear cells and hyperchromatic, basaloid cells with eosinophilic cytoplasm. No peripheral palisading and odontogenic apparatus was appreciated in any of the islands.^[12] Further negative PAS staining did not favour the diagnosis of clear-cell odontogenic carcinoma in our case.

It is exceedingly rare to find clear-cell changes in SCC arising from the oral epithelium and to the best of our knowledge, there have been very few case reports available in the English literature.

Clear-cell differentiation may be observed because of divergent clonal evolution within the neoplasm. Since there are very few case reports on clear-cell variant of oral squamous cell carcinoma, its prognosis is still vague and not obvious. Of the seven cases that have been reported

in the literature from skin, five had an aggressive growth feature. The single case reported from the oral cavity was seen on the lateral border of the tongue and was extremely aggressive.^[13] Our first case was a single primary lesion and though the patient did not show clinical evidence of metastasis at the time of presentation, he had to be immediately referred to the hospital for management of other complications like seizures which was diagnosed as metastatic deposits in brain, indicating the disseminated stage of cancer.

Clinical presentation of metastatic renal cell carcinoma in the oral cavity as first symptom of disease is very infrequent and suggests a very poor prognosis. Further, renal cell carcinoma is a malignant pathology of arduous and many times delayed diagnosis. In our case, the patient had first reported to dental OPD with a chief complaint of periapical cystic lesion in maxilla and was already undergoing chemotherapy for carcinoma of the abdomen. We envisaged that the primary lesion was in abdomen; however, microscopic picture made us suspect it as a clear-cell renal carcinoma, which was confirmed by tumour marker CD10 positivity. Therefore, it was a case of distant metastasis from kidney to the oral cavity.

Though renal cell carcinoma shows varied patterns histopathologically, clear-cell type occurs most frequently, accounting for 70% to 80% of renal cell cancers. On histologic examination, the tumours are made up of round or polygonal cells with clear or granular cytoplasm. The tumours have delicate branching vasculature and may exhibit cystic as well as solid areas. Most tumours are well differentiated, but some show marked nuclear atypia with formation of bizarre nuclei and giant cells. Unfortunately, one of the common characteristics of this tumour is its tendency to metastasize widely before giving rise to any local symptoms or signs.^[14]

CONCLUSION

We report two very unusual and intriguing cases of clear-cell carcinomas, one metastasized from the oral cavity to distant organs and the other exhibited metastasis to the oral cavity. Since both cases occurred in maxilla, which makes them exceedingly rare entities as clear-cell variant of oral squamous cell carcinoma as well as renal cell carcinoma have been documented to be located in the mandible.

Significantly, these case reports prompt us to comprehend the nature and biological behaviour of prevalent clear cells, that is, their presence makes the neoplasm more aggressive or not. Histopathologic diagnosis of clear-cell carcinoma warrants whole body clinical examination and immunohistochemical evaluation to provide timely treatment in view of dismal prognosis of such tumours.

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Conflicts of interest

There are no conflicts of interest.

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